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Luís Miguel Santos Costa

O Estilo de Vida e o Rim / Lifestyle and the Kidney

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À minha avó Alexandrina,

por todo o tempo que não estive consigo,

ao meu avô Manuel

por imaginar o orgulho que teria no seu neto

e aos meus pais

por tudo o que tenho

LIFESTYLE AND THE KIDNEY

ESTILO DE VIDA E O RIM

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ABSTRACT

Lifestyle refers to our daily behavior, attitudes and habits. Although not all lifestyle-defining components are under the control of the individual, some of them, such as nutrition, can be manipulated and adjusted to achieve positive health status goals. Diet and all its subcategories are concepts closely related to nutrition, presenting as vehicles for a beneficial and therapeutic approach in numerous pathological situations. The Vegetarian Diet is a specific type of diet that opposes the omnivorous diet by adopting a plant food base and rejecting meat, poultry and fish. The objective of this review is to systematize the current knowledge and definition of the nutritional characteristics of the Vegetarian Diet, as well as its comparison with the Non-Vegetarian Diet in general health, with special emphasis on health and function.

KEY-WORDS: Diet, kidney function, kidney health, lifestyle, vegetarian diet.

RESUMO

O estilo de vida refere-se ao nosso comportamento, atitudes e hábitos diários. Apesar de nem todos os componentes que definem estilo de vida estarem sob o controlo do indivíduo, alguns deles, como por exemplo a nutrição, podem ser manipulados e ajustados de forma a alcançar objectivos positivos para o estado de saúde. A dieta e todas as suas subcategorias são conceitos estreitamente relacionados com a nutrição, apresentando-se como veículos para uma abordagem benéfica e terapêutica em inúmeras situações patológicas. A Dieta Vegetariana é um tipo específico de dieta que se opõe à dieta omnívora por adotar uma base de alimentos de origem vegetal e rejeitar carne, aves e peixe. O objectivo desta revisão é a sistematização do conhecimento actual e definição das características nutritivas da Dieta Vegetariana, assim como a sua comparação com a Dieta Não-Vegetariana no estado de saúde geral, com especial ênfase na função e saúde renal.

PALAVRAS-CHAVE: Dieta, dieta vegetariana, estilo de vida, função renal, saúde renal.

INTRODUCTION

According to the World Health Organization, the concept of health is defined as a state of complete physical, mental and social well-being and not just the absence of disease [(1)]. It is a condition that will contribute to personal comfort and overall balance of the individual. Factors such as heredity, environment and lifestyle play a key role in structuring the health status [(2)]. Lifestyle is defined as the set of daily activities accepted as normal and conventional for each individual and encompasses the way they live, their attitudes, habits and behaviors in their daily lives. Although all the aspects that define lifestyle are not under the full control of the individual, it is possible to manipulate the influence that many of them have in our lives and therefore will affect our health and long-term well-being [(3)].

According to Donatelle, people experience throughout their development different activities, adopting habits that personally consider more satisfactory, and thus their lifestyle and network behavior are built [(3)]. The ultimate goal of this construction is reflected in the effort to maintain and promote health and prevent disease through specific behaviors that encompass five general categories: nutrition, socialization, mental stimulation, spirituality and physical activity [(4)]. All these categories and their effects on health are targets of intense study in the literature [(5)].

Nutrition is the process by which the necessary nutrients are obtained for a balanced state of health and growth. Closely related is the concept of diet, which includes the types of food a person, animal or community habitually consumes. Nutrition and diet can be used as therapeutic vehicles in order to preserve the health status of the individuals [(2)]. The interaction between the various organ systems and nutrition has a strong impact on the overall mortality [(6)], cardiovascular risk [(7)], the incidence of cancer [(8-10)], the risk of developing chronic diseases [(11, 12)] and neurodegenerative diseases [(13, 14)].

There are several types of diet, such as the Mediterranean diet, Nordic, DASH or Vegetarian diet (VD) for example [(15)]. The distinction between each type of diet depends on a large number of qualitative and quantitative combinations of different kinds of food [(16-18)]. The Mediterranean diet, characterized by a significant consumption of olive oil, vegetables, fruits and vegetables has a scarce content of saturated fatty acids and high load of monounsaturated fatty acids and fibers. On the other hand, the DASH diet was specifically designed to reduce blood pressure and maintain weight; is a diet rich in fruit, vegetables, dairy products and particularly low in saturated fatty acids and cholesterol, as well as a specific restriction of sodium [(15)]. These combinations will imply different effects on health status and prevention of disease.

VD is one of those possible combinations. It gained popularity over the years, with about 10% of the world population excluding red meat, poultry and fish from their eating habits [(19)] and replacing them with plant-based foods, being this the only requirement for defining a vegetarian [(20)]. There may be several subcategories of VD's depending on the food that is allowed on the diet (Table I).

VD have several advantages with proven effects on reducing the overall mortality [(21, 22)], reducing the incidence of ischemic heart disease, [(23)] inflammatory bowel disease, [(12)] type II diabetes mellitus [(24)], improvement in anthropometric and obesity parameters [(24)] and others (Table II); but also potential risks, notably by promoting nutritional deficiencies that can oppose the previous benefits [(25)].

The quality of diet and nutritional content are closely related to the kidney function [(26)]. In addition to protein load, the salt content also affects the progression of kidney disease. For example, a reduced-sodium diet delays chronic disease progression as opposed to diets rich in sodium and low in potassium that are associated with an increased risk of hypertension and renal injury [(27)].

Of the published articles that relate general dietary attitudes and the role of nutrition in kidney health [(11, 28-30)], few address the specific role of VD. Today we have the knowledge that VD's are beneficial in increasing the effectiveness of hemodialysis [(31, 32)], delaying the progression of chronic kidney disease [(33)] and reducing the number of nephrolithiasis acute events [(20)]. Nevertheless, many of the benefits of VD's on the nephrological system remain unclear [(34)].

This review proposes to summarize current knowledge of the effects of VD on health, discuss the main nutritional properties of this diet and compare the effects of two types of diet: VD and the Non-Vegetarian Diet (NVD) on renal function and health.

METHODS

Data collection was carried out through a systematic search of the literature on the Pubmed platform. There was no year of publication restriction nor language or type of study/article. Abstracts without full-texts were excluded, as were non-human studies. The terms used were "LIFESTYLE", "DIET" and/or "VEGETARIANISM".

In the first phase, articles that could have potential relevance were selected by evaluating their title and abstract, passing them to an evaluation of the full-text. Articles with no original or relevant content were excluded. The bibliography of each article included in the initial review was analyzed, and relevant titles or keywords that suggested potential information were included in this review.

VEGETARIAN DIETS AND THEIR SUBCATEGORIES

The categorization of a VD according to accepted or rejected food has different interpretations in the literature, such as the division of modern or classical VD's [15, 24]. This categorization is quite difficult due to the high number of subgroups and the fact that there aren't any truly distinguishing features between them [15].

Most of the current knowledge on the VD advantages results from studies of cohort with worldwide recognition, such as the European Prospective Investigation into Cancer and Nutrition-Oxford (EPIC-Oxford) and the Adventist Health (AHS) [35]. The cohort most generally used in the articles addressed in this review is the Adventist Health-2 (AHS-2). This recent study used a large sample of Seventh-day Adventists from the USA and Canada, which conferred a strong statistical power to study because of their positive health habits and low alcohol and tobacco consumption, thus reducing the non-dietary factors that could skew the results [23]. Non-dietary factors are one major limitation in the study of VD's as they difficult the dissociation of the VD's specific effects from other factors such as physical activity, smoking, alcohol consumption or BMI [36].

Because it is a cohort study with high quality standards and statistical power, the concepts of NVD, Semi-Vegetarian Diet (SVD), VD, Pesco-Vegetarian Diet (PVD), Lacto-Ovo-Vegetarian Diet (LOVD) and Vegan Diet (VGD) used throughout this review are the ones adopted by AHS-2 authors [22] and are set out in Table I.

NUTRITIONAL CHARACTERISTICS OF VEGETARIAN DIETS

For a proper diet comparison, it is important to be aware of the qualitative value of the prevalent nutrients in each type of diet [37]. The quantitative value does not assume an important role in our review because it depends on specific factors such as the type and amount of each food, the variation in the doses recommended by country and the individual characteristics of the individuals [24].

Awareness of the nutritious nature of the diet becomes essential to understand the various effects on health since they are directly dependent on changes in the nutritional content of the adopted diet [22, 37]. When a nutrient does not obtain adequate serum concentrations during a variable time interval nutritional deficiencies may occur, which are the main risk associated with VD [36]. On the other hand, there was a high resistance of vegetarian individuals to food supplements either by prejudice or by aversion, which can further complicate the objective of achieving an optimal serum concentration, although there is evidence of their effectiveness in the literature [37, 38].

In this segment of our review, we will describe some of the nutrients, vitamins and minerals characteristic of each diet. It is important to consider that the vegetarian subcategories are defined by the foods they do not contain, and so there may be significant differences in each nutrient [39].

Among the possible disadvantages of VD with particularly adverse consequences include reduced supply for n-3 long-chain fatty acids, cobalamin, iron, calcium and vitamin D (36). This concern is particularly emphasized for a VGD, in which nutritional deficiencies tend to be more severe (40).

Characteristics such as a high fiber content, folic acid, potassium, magnesium, and reduced levels of saturated fatty acids are principally responsible for the nutritional benefits of VD (36) (Table III).

Despite the nutritional differences, it is proven that the VD are suitable for any stage of the life cycle from childhood to old age, with normal growth in children and adolescents (19, 36) as long as adequate doses are provided.

OMEGA-3 FATTY ACIDS

Omega-3 polyunsaturated fatty acids (PUFAs), which include alpha-linolenic acid (ALA), linoleic acid (LA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), among others, are considered to have anti-inflammatory and anti-atherosclerotic properties as well as neuronal protection roles [(13)].

The PUFA may have two origins: derived from plants, such as flax seeds, hemp, nuts and vegetables [(41)] that can provide the ALA, but not the EPA and DHA; Or marine derivatives, primarily fish and seaweed, rich in EPA and DHA. Eggs and dairy products have low levels of EPA and DHA. The conversion of ALA to EPA and DHA can happen endogenously, but with a very small and limited rate, which is lower in males [(42)]. This conversion may be affected by several variables: tobacco has a positive effect as opposed to dietary linoleic acid (omega-6) which has a negative impact due to enzymatic competitive inhibition [(41)].

PUFAs, especially EPA and DHA, have a favorable influence on various organic systems due to improvement and prevention of dementia, prevention of memory and cognitive deficits, decreased production of cerebral inflammatory cytokines, maintenance of a positive mood state [(43)], decreased secretion of prostaglandin F-2alpha, reduced serum concentration of IL-6 and IL1beta, increased plasma concentration of transthyretin (TTR), increased secretion of sAPP-alpha, and other effects [(13)].

The low endogenous conversion rate justifies that people who do not consume fish, the main source of EPA and DHA, may have an increased risk of nutritional deficiency for these fatty acids. Studies on plasma levels of polyunsaturated fatty acids have consistently shown that vegetarians have generally lower levels of EPA and DHA, being lower than measured for NVD and DSV. DVG have even lower levels than DLOV [(13, 43)]. To avoid this nutritional deficit, it is recommended the regular consumption of foods rich in ALA (nuts and soybeans), fortified with DHA (soy milk and cereal) or DHA supplements [(44)].

VITAMIN B-12 - COBALAMINE

Vitamin B-12, also known as cobalamin, can be found essentially in animal source foods, being virtually non-existent in plant source foods. Besides this, the process of preparing food, cooking, pasteurization or exposure to fluorescent light can lead to losses up to 50% of cobalamin content [45].

Although cobalamin is present in dairy products and eggs, the quantity is not sufficient to ensure the recommended minimum, even if consumed daily [46], thereby increasing the risk of serious deficiencies for health, though these rarely occur [36]. For individuals who do not consume any source of cobalamin the only feasible way to achieve an optimum concentration is by combining dairy products, eggs, fortified food or dietary supplements [46].

Cobalamin is essential for the synthesis of purines and pyrimidines, the conversion of methylmalonyl CoA to Succinyl CoA, the conversion of homocysteine to methionine, among other functions [47]. The cobalamin deficiency may have several consequences: hyperhomocysteinemia, especially in women, which is an important cardiovascular risk factor [24], increased mean corpuscular volume with the development of megaloblastic anemia [47], increased risk of cardiovascular events [48], cerebral atrophy and dementia [14], depression [49], deficits in bone mineral density [50] and neuronal tube defects [51]. Even with low serum levels, cobalamin deficiency in VD with hematological and brain damage are rare and only are known to have occurred in VGD [36].

IRON

Iron is considered a critical nutrient for VD [24]. There are two forms of iron in food presentation: heme iron, which is derived primarily from hemoglobin and animal myoglobin, has high bioavailability and is not influenced by factors that inhibit intestinal absorption, such as phytic acid [52]; non-heme iron can be found in cereals, bread, vegetables, dried fruits, seeds, nuts and dark green leafy vegetables. Non-heme absorption and bioavailability are considerably lower [53], being largely dependent on factors that inhibit luminal absorption such as amino acids, ascorbic acid, citric acid and hydrochloric acid [19].

The amount of iron present in NVD and VD is very similar, being the bioavailability of each type of iron the main difference (20). In animal products, about 40% of the total amount of iron appears as heme iron and the remaining 60% non-heme iron, in contrast to the presentation for plant products as non-heme iron only (53). The serum ferritin is lower in vegetarian subjects as compared to non-vegetarian while hemoglobin levels and hematocrit are similar or slightly lower (44).

Under normal conditions, this difference is not significant (24) because despite having a lower store of iron the VD does not have a higher incidence of iron deficiency anemia (24). This may be justified because of the high consumption of vitamin C in the VD, which was proved to increase the absorption of non-heme iron (44).

In some specific situations such as growth, pregnancy, high demand for iron, and depletion of reserves by hemorrhage, trauma and bleeding, there may be an increased risk of iron deficiency anemia (52). In these situations, dietary supplementation with iron and vitamin C to increase absorption may be necessary (20).

VITAMIN D

Vitamin D is essential for increasing the efficiency of calcium metabolism, especially when consumption is reduced (19). VD contains lower serum levels of vitamin D compared with NVD. This association is stronger for VGD (44).

Only vegans, elderly people and people with limited sunlight exposure who do not consume fortified foods with vitamin D need nutritional compensation (54). If inadequate, as in the case of vegans who neglect their diet supplementation or do it irregularly (38), a nutritional deficit can surface with consequent loss of bone mineral density (19, 44).

CALCIUM

Milk and dairy contribute to over 50% of ingested calcium (55). For this reason LOVD have adequate intakes of the mineral (19). The only diet that can establish deficits in calcium intake is the

VGD diet because of its exclusion of dairy products, eggs and even small animal bones such as sardines, salmon or small birds [19].

High fiber consumption, characteristic of the VGD diet, including its components: oxalic acid (spinach) and phytic acid (cereal) may contribute to an inhibition of intestinal absorption of calcium, placing vegans in a particularly susceptible position to deficits of this mineral [19].

CHOLESTEROL

The serum values of total cholesterol and LDL cholesterol are lower in VD when comparing with NVD [39, 56]. The PVD have similar LDL levels to vegetarians [56]. HDL cholesterol has higher serum levels in PVD although no significant difference was found among other types of vegetarian diet [56].

The effect of diets on serum cholesterol depends on the exact composition of the diet and the foods that define it. A VD containing a portfolio of foods shown to reduce cholesterol, such as nuts and soy, will register lower LDL cholesterol serum values when compared to a VD without these foods [20].

PROTEINS

Protein intake being lower in VD comparing to NVD is a consistent finding in literature, however, the daily recommended dose is provided in both of them thus reducing the risk of protein insufficiency even at any stage of Chronic Kidney Disease (CKD) [44, 57]. The energy supply of protein source is also lower in DV although there is no risk of energy failure [57].

FIBERS

VD has a substantially higher fiber content than NVD. This is explained by the larger consumption of fruits, vegetables and cereals [58]. The fibers show protective properties against various types of cancer [44] cardiovascular disease, [37] Crohn's disease [12], Non-alcoholic steatohepatitis as well as a reduction in mortality in patients with CKD [59].

ZINC

Vegetarians may be at risk for a nutritional deficit of zinc [44] due to the low amounts of this mineral in the dietary pattern of VD [36]. This mineral is mainly present in meat, eggs and seafood [19]. The fact that the phytic acid of seeds and vegetables binds to zinc and reduces its bioavailability [44] justifies the nutritional risk. Despite this difference in bioavailability, functional immunocompetence of individuals does not vary between VD and NVD thus establishing the hypothesis of the existence of compensation mechanisms that protect vegetarians from this deficit [60].

VEGETARIAN DIET AND THE ORGANIC SYSTEMS

VD interacts with different organ systems with mortality being a good indicator to summarize the overall effect of VD in the human body [21]. If we use all-cause mortality to compare different types of diet we can verify that in general there is a lower mortality associated with VD compared to NVD [22]. The specific mortality of renal and endocrine causes, respectively renal failure and diabetes mellitus type II (DMII), is also significantly lower in vegetarians (Table II). If we compare gender there is a significant difference as overall mortality is lower in male individuals [22].

VEGETARIAN DIET AND CARDIOMETABOLIC RISK

One of the main advantages of VD, which contributes to a reduction in overall mortality rate, is the lower mortality from ischemic heart disease and protection against cardiometabolic risk factors including obesity, hypertension, dyslipidemia and DMII [24, 36].

Some cohort studies have shown a 2-4-point reduction in the body mass index of vegetarians compared to non-vegetarians, reflecting a lower incidence of obesity and obesity-related diseases, which are a major cause of morbidity and mortality [20, 23].

VD present lower basal blood pressure values, and there is a significant reduction in this parameter in hypertensive non-vegetarian subjects who change their diet for VD [36].

Insulin resistance is associated with atherosclerosis and increased cardiovascular mortality in the general population [36]. Vegetarian individuals are more sensitive to insulin than non-vegetarians, being this sensitivity correlated with the number of years of vegetarianism. Glucose levels and endogenous glucose production is also decreased in VD [36]. The incidence of metabolic syndrome and DMII in all VD is lowered being VGD the most significant association [23].

VEGETARIAN DIET AND DEPRESSION

Depression is a multifaceted condition with various biological and environmental causes that is associated with an increased risk of developing cardiovascular disease, diabetes, epilepsy, stroke, dementia, and cancer [61]. Due to these increased risks, depression is an important target of many studies searching associations with VD.

Nutrition and depression are highly correlated due to an activation of neural and hormonal pathways in the gastrointestinal tract that modulates brain functions such as cognition, appetite, sleep and mood [61]. Omega-3 fatty acids show some effect on initializing and stabilizing a positive mood [61]. Despite having lower levels of EPA and DHA, vegetarians do not have a higher risk for depression either negative mood states, even reaching higher scores than NVD subjects [43]. These results are contradictory to what is known about the association between dietary fatty acids and brain function, suggesting an unknown benefit of VD on the mood state [43].

VEGETARIAN DIET AND ONCOLOGICAL RISK

The content of VD, rich in fiber, vitamin C, and flavonoids, antioxidants with an important antiproliferative activity, suggests that VD could theoretically interfere with incidence and neoplastic progression [36]. The fact that the consumption of red meat was associated with an increased incidence of gastrointestinal cancers [8] also potentiated the idea of the possible benefit VD had on cancer prevention.

This assumption was explored and it was found that the overall neoplastic risk is reduced in VD although results are inconclusive for specific cancers other than colorectal cancer, which has a reduced risk especially in DPV and DLOV [9, 20]. DVG is associated with a reduced incidence of female-specific cancers [62].

VEGETARIAN DIET AND BONE HEALTH

Although there is intensive research in the literature, the relationship between VD and bone health is not well clarified due to many different outcomes in several studies [20]. A meta-analysis of nine studies found that bone mineral density of the femoral neck and lumbar spine was 4% lower in vegetarian subjects [20]. Cohort EPIC-Oxford data reveal no differences in the incidence of fractures, except for VGD which had a 30% higher risk of fracture [20]. Data from AHS-2 showed there was a greater risk of hip fractures in both sexes for individuals who did not consume meat regularly [20].

VEGETARIAN DIET AND OTHER PATHOLOGIES

VD can also be associated with several other pathologies: vegetarians have a very significant reduction in the incidence of colon diverticular disease, with a 72% lower risk in VGD; the risk of cataracts, degenerative arthritis and hyperthyroidism also follows the same trend [20].

VEGETARIAN DIETS AND RENAL HEALTH

RENAL FUNCTION MARKERS

The relationship between the consumption of various foods and corresponding nutritional composition with renal function, including glomerular filtration rate (GFR) is one of the most important questions on this subject [63]. A combination of nutrients which could reduce GFR decline would be a great therapeutic approach to CKD because of the powerful association between small decreases in GFR and renal disease, cardiovascular risk and all - cause mortality [63].

The comparison between VD and NVD in a Taiwanese population showed no significant difference in GFR and renal function [64], but the published literature for this relationship is very limited. Although the role of dietary protein in the reduction of GFR decline is controversial, a small advantage was registered, being more evident in diabetic subjects [63]. Higher sodium consumption is consistently associated with declines in GFR, but it is assumed that elevated blood pressure due to higher salt load may play a major role in this variation [63]. The β-carotene, present in roots and tubers, is also seen as a possibility to reduce the risk of decline in GFR [63]. Both low sodium and β-carotene intake have a similar positive association with the GFR in diabetic and non-diabetic subjects, this being higher when considering a cumulative consumption over several years [63].

The NVD possess higher blood urea nitrogen (BUN) serum values than VD, possibly due to a higher protein intake, as well as higher serum creatinine ratio and urea/creatinine ratio [34].

MICROALBUMINURIA

Microalbuminuria (MA) is also an important indicator of kidney disease [63]. The NVD have higher levels of urinary albumin excretion compared to the VGD [34]. Diets low in protein, animal fat and cholesterol play a protective role for MA. The use of two or more servings of red meat per day was correlated with an increased risk of 50%, highlighting the important role of VD in the prevention of MA [63]. Also relevant is the association of VGD to systemic hemodynamic and glomerular changes that may be beneficial in preventing glomerular sclerotic changes [34].

CHRONIC KIDNEY DISEASE

One of the most frequently addressed pathological entities on literature and with a greater impact on the health of general population is CKD [11, 28]. It is characterized by a set of clinical signs of renal damage and proteinuria and/or a reduction in GFR [65]. The definition assumes that the development of end-stage renal disease can be prevented or delayed through detection and treatment of early renal disease [66].

The development of proteinuria has a clear relationship with factors such as obesity, hypertension and DMII, all of which relate positively with VD as mentioned in the previous segment of our review [66].

The literature suggests that low-protein diets retard the progression of CKD [33]. This data is useful to support the use of VD in patients with renal impairment and are concordant with current nutritional recommendations for patients with CKD that suggest a reduction in protein intake [36]. The safety of VD to all individuals, especially pregnant women with CKD, a highly challenging situation, was also confirmed in a 2011 study. Women maintained adequate nutritional status during pregnancy and after childbirth, as well as their infants, who presented a normal intra-uterine growth [36].

Shifting from NVD with animal proteins to a VD especially rich in soy proteins also shows positive effects on blood pressure and lipid profile, as well as reduced proteinuria and improved renal perfusion with less damage in patients with CKD [64].

HYPERPHOSPHATEMIA

Hyperphosphatemia is an independent risk factor for mortality in patients with CKD and undergoing dialysis. In these patients, hyperphosphatemia results from a positive phosphorous balance in spite of secondary hyperparathyroidism and an increase in fibroblast growth factor 23 (FGF23) as a compensatory effort [36]. FGF23 is an important independent risk factor for increased risk of cardiovascular events and overall mortality [36]. VD is associated with lower serum levels of phosphorus, FGF23 and urinary phosphorus excretion when compared to NVD [36].

HYPERKALEMIA

Diets rich in plant foods can be theoretically harmful to CKD patients because of its high potassium content, but real risk of hyperkalemia is reduced due to the alkaline properties of this type of diets. Although small, this risk must not be undervalued in patients with low values of GFR [36]. Metabolic acidosis and hypertension in patients with CKD stage 4 can be corrected with an increase of fruit and vegetables in the diet without a significant increase in the incidence of hyperkalemia [67].

METABOLIC ACIDOSIS

There is strong evidence that diet is related with acid-base homeostasis [68]. In general, a high protein intake is associated with a greater acid load, while fruits and vegetables are associated with a high content of bicarbonate producing anions such as citrate and lactate, thus decreasing renal acid load [36, 68].

VD's are more effective at correcting metabolic acidosis in patients with CKD than the administration of isolated bicarbonate, as opposed to animal protein-rich NVD which may exacerbate acidosis [67]. In addition to the correction of an acidotic state, vegetarian showed benefits to two main parameters in the progression of CKD: hypertension and proteinuria in patients with CKD Stage 2 and hypertensive nephropathy [36].

INTESTINAL MICROBIOME

Intestinal microbiome is liable to be manipulated by the type of diet adopted [67]. A disruption to intestinal symbiosis is observed frequently in populations with kidney disease, contributing to an accumulation of uremic toxins with cardiovascular risks, such as sulfate indoxyl (IS) and p-cresyl sulfate (PCS) which result from intestinal bacterial metabolism of tryptophan and tyrosine respectively [31, 67]. Populations who adopt VD rich in fiber, fruits and vegetables, have a greater abundance of healthy microbiome and lower production of IS and PCS compared to an NVD poor in fiber and with greater consumption of meat [31, 67].

HEMODIALYSIS

Nutritional status is one of the most important predictors of mortality and morbidity in patients on hemodialysis (HD) [69]. For this reason, it is essential to understand the relationship between the type of diet and nutritional status of patients with HD quality. Despite VD not supplying the recommended protein amount for HD, there is no commitment to the quality of the procedure, even if there are small changes to anthropometric markers and hematocrit [36]. These changes to the hematocrit can be neutralized by a higher dose of erythropoietin [69].

Dialysis patients have a higher cardiovascular risk due to the retention of advanced glycation end-products (AGE). The amount of tissue AGE can be measured by skin autofluorescence (APS), an effective method of measuring chronic exposure to AGE, rather than serum levels. The accumulation of AGE occurs due to an endogenous production and exogenous intake of protein and fat associated with reduced renal clearance. Comparison of SAF dialyzed individuals in VD and NVD groups concluded that vegetarian had lower values of AGE tissue deposit. Therefore, in dialysis patients with reduced renal clearances, VD proved beneficial in lowering the amount of exogenous AGE [70].

NEPHROLITHIASIS

The literature suggests that in general, VD have a lower risk of kidney stones compared to NVD [20], and only VGD raises doubt to the negative interaction between micro-nutrition deficits and hyperuricemia to the prevention of nephrolithiasis [40]. This reduced risk is more exuberant for LOVD if a simultaneous and adequate content of calcium and oxalate and not excessive fiber content is provided [40].

CONCLUSION

The amount of information about the benefits of VD on health is not extensive, but the literature to date suggests that these diets are associated with better health outcomes in the long-term compared to non-vegetarians. VD emerges as a healthy and nutritionally appropriate option for all stages of life, including pregnancy, childhood, adolescence and adulthood, as well as beneficial in the prevention of several chronic diseases.

This dietary approach has reduced levels of saturated fatty acids, cholesterol, sodium, and animal protein, associated with a high amount of beneficial nutrients such as fibers, magnesium, potassium, carbohydrates and antioxidants such as vitamin C. The risk of nutrient deficiencies, although rare and most likely to happen in vegans, exists primarily to omega-3 fatty acids, cobalamin, iron, vitamin D and calcium. Vegetarians can avoid nutritional deficits if they have knowledge about the possible nutritional risks of their diet and make good food choices with consumption of foods rich in the missing nutrients, fortified foods or dietary supplementation.

A lower overall mortality associated with a reduction of cardiometabolic risk, overall cancer, colon diverticular disease, cataracts, degenerative arthritis and hyperthyroidism should raise awareness to the benefits of VD and their impact on general health. The relationship between kidney health and VD, although still not well clarified, already reveals important implications. The possibility to reduce GFR decline through VD should be a big reason for further study on this subject. VD are shown to be nutritionally safe in all individuals with CKD and present many benefits like an increased efficiency of hemodialysis, correction of metabolic acidosis, reduction of hyperphosphatemia, nephrolithiasis episodes, microalbuminuria and finally a delay in the natural progression of CKD.

Our review suggests that dietary modification to vegetarian options can be presented as an important strategy for maintaining kidney health, although we need more studies to better understand the possibilities that VD can provide us.

DISCLOSURE

The authors have no conflicts of interest to declare.

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TABLE I. Diet types definition according to AHS-2*

TYPE OF DIET	DEFINITION	MEAT	POULTRY	FISH	DAIRY/EGGS
NVD[ac]	Meat, poultry, fish, dairy and eggs more than once a week				
SVD[c]	Meat, poultry, fish, dairy and eggs less than once a week but more than once a month				
VD	**Base of plant foods. Rejects meat, poultry and fish. May have several subcategories depending on the foods the diet allows**				
PVD	Fish, dairy and eggs but rejects meat and poultry				
LOVD	Dairy and eggs but rejects meat, poultry and fish				
VGD[b]	Rejects meat, poultry, fish, dairy and eggs				

* Color gradation from red to dark green corresponds to an increase in consumption of the selected foods, with red being the complete rejection. NVD (Non-vegetarian Diet), SVD (Semi-vegetarian Diet), VD (Vegetarian Diet), PVD (Pesco-vegetarian Diet), LOVD (Lacto-ovo-vegetarian Diet) e VGD (Vegan Diet) [a] can also be called Omnivorous Diet [64] [b] can also be called Restrictive Vegetarian Diet [19] [c] may include plant-based foods.

Adapted from Le LT, Sabate J. *Beyond meatless, the health effects of vegan diets: findings from the Adventist cohorts*. Nutrients. 2014;6(6):2131-47

TABLE II. Association between diet types and general and specific mortality in Hazard Ratio (95% CI) among participants (N = 73 308) of AHS-2 (2002-2009)*

DIET	GENERAL	IHD	CVD	CANCER	INFECT.[a]	NEURO.[b]	PNEUMO.[c]	RENAL[d]	ENDOC.[e]
NVD	1[Reference]	1[Reference]	1[Reference]	1[Reference]	1[Reference]	1[Reference]	1[Reference]	1[Reference]	1[Reference]
SVD	0.92 (0.75-1.13)	0.92 (0.57-1.51)	0.85 (0.63-1.16)	0.94 (0.66-1.35)					
VD					0.93 (0.53-1.62)	0.93 (0.67-1.29)	0.95 (0.68-1.32)	0.48 (0.28-0.82)[f]	0.61 (0.40-0.92)[f]
PVD	0.81 (0.69-0.94)[f g]	0.65 (0.43-0.97)[f h]	0.80 (0.62-1.03)[g]	0.94 (0.72-1.22)					
LOVD	0.91 (0.82-1.00)[f]	0.82 (0.62-1.06)	0.90 (0.76-1.06)[g]	0.90 (0.75-1.09)					
VGD	0.85 (0.73-1.01)[g]	0.90 (0.60-1.33)[g]	0.91 (0.71-1.16)[g]	0.92 (0.68-1.24)					

* All values are adjusted to age, exercise, tobacco consumption, monetary income, civil status, education level, alcohol consumption, sleep hours and geographical region. NVD (Non-vegetarian Diet), SVD (Semi-vegetarian Diet), VD (Vegetarian Diet), PVD (Pesco-vegetarian Diet), LOVD (Lacto-ovo-vegetarian Diet) e VGD (Vegan Diet), IHD (Ischemic Heart Disease) e CVD (Cardiovascular Disease).

[a b c d e f g h] Most common causes of specific mortality for each category in decreasing order of frequency: [a] Septicemia [b] Alzheimer's Disease; Parkinson's Disease [c] Influenza and Pneumonia; Emphysema and Chronic Obstructive Pulmonary Disease; Interstitial Pulmonary Disease [d] Renal Failure [e] Diabetes Mellitus [f] Statistically significant values for both genders marked in green [g] Statistically significant values for males [h] Statistically significant values for females.

Adapted from Orlich MJ, Singh PN, Sabate J, Jaceldo-Siegl K, Fan J, Knutsen S, et al. *Vegetarian dietary patterns and mortality in Adventist Health Study 2*. JAMA Intern Med. 2013;173(13):1230-8

TABLE III. Mean (± standard deviation) energetic and nutrient intake for non-vegetarian premenopausal women and vegetarian women*

ENERGY AND NUTRIENT		NVD (n=22)	VD (n=23)	LOVD (n=15)[a]	VGD (n=8)
Energy	kcal	2.086±528	1.989±469	2.024±548	1.923±290
Proteins	g	77.1±19.7	55.3±11.3[d]	57.1±10.8	51.9±12.1
	% energy	14.8±2.3	11.1±2.0[d]	11.5±2.1	10.4±1.6
Carbohydrates	g	284.0±77.4	292.2±67.6	288.3±79.8	299.5±38.8
	% energy	54.0±4.6	57.6±5.2	55.9±4.5	60.9±5.1
Fibers	g	22.4±7.2	28.3±9.8[b]	24.7±7.9	35.0±9.9
Fatty acids	g	75.0±23.2	71.6±24.1	75.5±24.7	64.3±22.4
Saturated	g	25.2±11.3	20.8±9.1	23.8±8.6	15.1±7.5
Monounsaturated	g	28.4±9.0	27.4±9.9	28.3±9.5	25.9±11.0
Polyunsaturated	g	14.6±3.6	16.5±6.3	16.1±6.1	17.3±6.9
P:S Ratio**		0.64±0.21	0.93±0.59[b]	0.70±0.25	1.36±0.81
Cholesterol	mg	231±87	132±82[d]	152±77	94±83
Thiamine	mg	1.55±0.41	1.49±0.55	1.31±0.40	1.83±0.67
Vitamin B-12	µg	3.79±1.60	1.15±0.78[d]	1.49±0.72	0.51±0.41
Vitamin C	mg	116±39	156±62[b]	141±66	186±45
Calcium	mg	950±437	771±270	875±255	578±184
Iron	mg	15.3±4.9	15.1±4.8	13.7±4.8	17.7±3.8
Magnesium	mg	303±91	358±106	337±109	396±92
Zinc	mg	11.1±3.9	8.3±2.1[c]	8.2±2.2	8.5±2.2
Sodium	mg	2.789±757	2.210±771[b]	2.175±801	2.275±770
Potassium	mg	3.042±833	3.128±854	2.884±742	3.587±908

* NVD (Non-vegetarian Diet), VD (Vegetarian Diet), LOVD (Lacto-ovo-vegetarian Diet), VGD (Vegan Diet)

** Polyunsaturated fatty acids to saturated fatty acids racio

[a] of 15 LOVD, 11 included eggs in their diet [b] P<0.05 color orange [c] P<0.01 color blue [d] P<0.001 green color

Adapted from Janelle KC, Barr SI. Nutrient intakes and eating behavior scores of vegetarian and nonvegetarian women. J Am Diet Assoc. 1995;95(2):180-6, 9, quiz 7-8.

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ANEXOS

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Examples

1. *Journals*:
Hogan J, Mohan P, Appel GB. Diagnostic tests and treatment options in glomerular disease: 2014 update. Am J Kidney
Dis 2014;63(4):656-666

2. *Books*:
Morris Peter, Knechtle Stuart. Kidney Transplantation - Principles and Practice. 7th Edition. Saunders, 2014:72

3. *Website*:
Substitutive Renal Therapy of Chronic Renal Disease in Portugal.
Available at http:www.spnefro.pt/comissoes_Gabinete_registo_2013/registo_2013.
Accessed October 6, 2013.

4. *Published Meeting Abstract*:
Jorge Silva, Jorge Antunes, Telmo Carvalho, Pedro Ponce.
Efficacy of preventing hemodialysis catheter infections with citrate lock (Encontro Renal abstract SE001). Port J Nephrol Hypert 2011; 25(1):56

Tables: Tables should supplement, not duplicate, the information in the main text. References to tables should be made in order of appearance in the text and should be in Roman numerals in brackets, e.g. (Table II). Each table should be typed on a separate sheet and have a brief heading describing its contents.

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